A hESc-based Development Candidate for Huntington's Disease

Grant Award Details

A hESc-based Development Candidate for Huntington's Disease

Grant Type: Early Translational II

Grant Number: TR2-01841

Project Objective: Systematic analysis of hESC derived SC candidates(hNSC, hNPC and hAPC) for the treatment of Huntington's disease. POC in an aggressive model of HD (R6/2 120 repeat) will be first tested with all candidates. The best candidate will then be moved forward into longitudinal studies in a longer surviving (less aggressive) murine model of HD.
Questions that will be tackled during the project
1) Will benefits persist and provide longterm benefit, 2) Which one will provide optimal protection: restricted or more multipotent cells? 3)do transplanted cells modify disease phenotype via direct or indirect mechanisms?

Investigator:

Name:	Leslie Thompson
Institution:	University of California, Irvine
Type:	PI

Disease Focus: Huntington's Disease, Neurological Disorders

Human Stem Cell Use: Embryonic Stem Cell

Cell Line Generation: Embryonic Stem Cell

Award Value: $3,955,038

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 2

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Reporting Period: Year 3

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Reporting Period: Year 4/NCE/Bridge

View Report

Grant Application Details

Application Title: A hESc-based Development Candidate for Huntington's Disease

Public Abstract: Huntington's disease (HD) is a devastating degenerative brain disease with a 1 in 10,000 prevalence that inevitably leads to death. These numbers do not fully reflect the large societal and familial cost of HD, which requires extensive caregiving. HD has no effective treatment or cure and symptoms unstoppably progress for 15-20 years, with onset typically striking in midlife. Because HD is genetically dominant, the disease has a 50% chance of being inherited by the children of patients. Symptoms of the disease include uncontrolled movements, difficulties in carrying out daily tasks or continuing employment, and severe psychiatric manifestations including depression. Current treatments only address some symptoms and do not change the course of the disease, therefore a completely unmet medical need exists. Human embryonic stem cells (hESCs) offer a possible long-term treatment approach that could relieve the tremendous suffering experienced by patients and their families. HD is the 3rd most prevalent neurodegenerative disease, but because it is entirely genetic and the mutation known, a diagnosis can be made with certainty and clinical applications of hESCs may provide insights into treating brain diseases that are not caused by a single, known mutation. Trials in mice where protective factors were directly delivered to the brains of HD mice have been effective, suggesting that delivery of these factors by hESCs may help patients. Transplantation of fetal brain tissue in HD patients suggests that replacing neurons that are lost may also be effective. The ability to differentiate hESCs into neuronal populations offers a powerful and sustainable alternative for cell replacement. Further, hESCs offer an opportunity to create cell models in which to identify earlier markers of disease onset and progression and for drug development.

We have assembled a multidisciplinary team of investigators and consultants who will integrate basic and translational research with the goal of generating a lead developmental candidate having disease modifying activity with sufficient promise to initiate IND-enabling activities for HD clinical trials. The collaborative research team is comprised of investigators from multiple California institutions and has been assembled to maximize leverage of existing resources and expertise within the HD and stem cell fields.

Statement of Benefit to California:	The disability and loss of earning power and personal freedom resulting from Huntington's disease (HD) is devastating and creates a financial burden for California. Individuals are struck in the prime of life, at a point when they are their most productive and have their highest earning potential. As the disease progresses, individuals require institutional care at great financial cost. Therapies using human embryonic stem cells (hESCs) have the potential to change the lives of hundreds of individuals and their families, which brings the human cost into the thousands. For the potential of hESCs in HD to be realized, a very forward-thinking team effort will allow highly experienced investigators in HD, stem cell research and clinical trials to come together and identify a lead development candidate for treatment of HD. This early translation grant will allow for a comprehensive and systematic evaluation of hESC-derived cell lines to identify a candidate and develop a candidate line into a viable treatment option. HD is the 3rd most prevalent neurodegenerative disease, but because it is entirely genetic and the mutation known, a diagnosis can be made with certainty and clinical applications of hESCs may provide insights into treating brain diseases that are not caused by a single, known mutation. We have assembled a strong team of California-based investigators to carry out the proposed studies. Anticipated benefits to the citizens of California include: 1) development of new human stem cell-based treatments for HD with application to other neurodegenerative diseases such as Alzheimer's and Parkinson's diseases that affect thousands of individuals in California; 2) improved methods for following the course of the disease in order to treat HD as early as possible before symptoms are manifest; 3) transfer of new technologies and intellectual property to the public realm with resulting IP revenues coming into the state with possible creation of new biotechnology spin-off companies; and 4) reductions in extensive care-giving and medical costs. It is anticipated that the return to the State in terms of revenue, health benefits for its Citizens and job creation will be significant.